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Gender Differences in the Incidence of Coronary Artery Disease in Patients With Stable Angina and Positive or Negative Stress Test in Daily Clinical Practice in the Year 2002: Results of the ALKK Quality Control Registry

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Objective: To evaluate the impact of gender on prevalence of CAD (any coronary stenosis $\geq 50\%$) in patients with stable angina and stress test performed before angiography. **Methods:** In 2002 a total of 123,328 consecutive invasive procedures in 81 hospitals of the ALKK were prospectively included into the ALKK quality control registry. 33% of patients were female, mean age was 65 years. From these 48,617 patients had stable angina with a positive ($n=32,506$; 66.8%) or negative ($n=16,111$; 33.2%) stress test before angiography.

Results:

Table 1: Positive stress test

	Male (n=21734)	Female (n=10772)	p-value
No CAD	16.2 %	33.5 %	<0.0001
CAD	78.2 %	54.5 %	<0.0001
Other cardiac disease	5.6 %	12.0 %	<0.0001

Table 2: Negative stress test

	Male (n=10602)	Female (n=5509)	p-value
No CAD	25.7 %	41.5 %	<0.0001
CAD	63.8 %	44.2 %	<0.0001
Other cardiac disease	10.5 %	14.3 %	<0.0001

Conclusions: In patients with stable angina the incidence of a false positive stress test is double as high in women as in men. Stress testing has a significantly lower positive but a higher negative predictive value for CAD in women.

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Prognostic Value of Circulating B-Type Natriuretic Peptide in Patients With Stable Coronary Artery Disease

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Background: B-type natriuretic peptide (BNP) levels are strong predictors of survival in patients with acute coronary syndromes and in patients with congestive heart failure. Whether plasma concentrations of B-type natriuretic peptide (BNP) are predictive of long-term survival in patients with angiographically documented, clinically stable coronary artery disease is unknown.

Methods: 197 patients with stable angina pectoris and angiographic evidence of significant coronary artery disease were included. Patients with a recent myocardial infarction, electrocardiographic evidence of ongoing ischemia, anginal pain at rest, or symptomatic congestive heart failure were excluded.

Results: During a median follow-up of 52 months, 9 patients died. Plasma BNP levels were significantly higher in non-survivors than in survivors ($28.0 (\pm 19.5)$ vs $17.8 (\pm 12.2)$ pmol/L; $p=0.036$). By logistic regression a history of diabetes mellitus ($p=0.003$), the presence of pathological Q-waves on the electrocardiogram ($p=0.024$), and baseline BNP levels ($p=0.032$) were identified as significant predictors of all-cause mortality. In a stepwise multivariate model, diabetes mellitus ($p=0.002$) and BNP ($p=0.015$) were identified as independent prognostic indicators.

Conclusions: In patients with clinically stable, angiographically documented coronary artery disease, plasma BNP provides prognostic information beyond that obtained from standard risk markers. BNP determination may have a role in risk stratification in this large and important patient group.

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Protective Role of Low C-Reactive Protein Levels Against Classical Risk Factors for Coronary Atherosclerotic Disease

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Background: Despite the presence of multiple traditional risk factors some patients do not develop significant coronary atherosclerosis (CAD). We studied the prevalence of this phenomenon in order to search for possible protective factors against the deleterious effects of multiple risk factors.

Methods: Out of 1890 consecutive patients (pts) with stable angina admitted for elective coronary angiography, between January 1998 to December 1999, we identified 84 pts with 3 or more conventionally defined risk factors (hypercholesterolemia, diabetes, hypertension, obesity, smoking, family history of CAD) and a normal coronary angiography. All angiographies were then reviewed quantitatively (Medis QCA). 44 pts (group A) had completely normal arteries (23 male, range 38-76 years old; risk factors: 75% family history, 23% diabetes, 68% hypercholesterolemia, 70% smoking, 75% hypertension, 23% obesity).

As a control group we selected in our clinical database 44 pts (group B), matched for sex, age and risk factors, with multivessel ($> 70\%$ stenosis) CAD, clinically stable for more

than 6 months. Blood levels of hs-CRP and HDL and LDL cholesterol were measured in all pts.

Results: As expected from the inclusion criteria, no difference was observed between group A and B in classical risk factors prevalence and blood cholesterol levels (mean \pm SD; HDL 41.7 ± 9.8 mg/dl vs 43.5 ± 13.2 mg/dl and LDL 136.1 ± 35.0 mg/dl vs 141.0 ± 43.7 mg/dl respectively). Conversely there was a statistically significant difference between the hs-CRP values between group A and B (median and 25th-75th percentile respectively 1.97 mg/l; 0.93-4.73 mg/l vs 2.97 mg/l, 1.61-5.06 mg/l; $p < 0.05$).

Conclusions: Despite the presence of multiple coronary risk factors, pts with low hs-CRP values may have angiographically normal coronary arteries, suggesting that a chronic subclinical inflammation may be a necessary condition for the development of angiographically detectable coronary atherosclerosis.

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Immunoglobulin A Anticardiolipin Antibodies Are Markers of the Extent of Daily Life Ischemia in Patients With Stable Angina

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Anticardiolipin antibodies (ACA) present procoagulant activity and cause significant endothelial dysfunction when binding on the cell surface. We investigated whether ACA plasma levels are related to platelet activation, thrombin generation and daily life ischaemia in patients with stable angina (SA).

METHODS: We measured (mean \pm SE) IgG, IgM, IgA ACA plasma levels (mg/dl), prothrombin fragments (PF1+2, nmole/l), 24h urine excretion of 11-dehydrothromboxane B2 (DHTXB2, ng/ml, creatinine) in 60 patients with SA and in 20 matched for age and atherosclerotic risk factors controls. Patients had angiographically documented disease and underwent a 48h Holter monitoring for assessment of the number and duration of ischaemic episodes.

RESULTS: Patients had higher IgA-ACA plasma levels than controls (4.3 ± 0.45 vs 2.2 ± 0.17 , $p < 0.01$). Increased IgA-ACA were related to increased number and duration of ischaemic episodes ($r=0.41$ and $r=0.48$, respectively, $p < 0.01$). Patients with > 10 ischaemic episodes ($n=14$) or duration of ischaemia > 30 min ($n=18$) had higher IgA ACA than those with < 10 episodes or < 30 min duration (6.4 ± 0.9 vs 3.4 ± 0.4 , $p=0.007$ and 5.6 ± 0.7 vs 3.2 ± 0.5 , $p=0.018$ respectively). ROC curve analysis showed that IgA-ACA levels > 3.4 mg/dl predicted a number of ischaemic episodes > 10 or duration of ischaemia > 30 min with 75% and 78% sensitivity and 80% and 63% specificity (area: 0.80, CI: 0.63-0.96, $p=0.006$ and area: 0.78, CI: 0.58-0.94, $p=0.001$ respectively). High IgA-ACA levels were related to reduced platelet count and 11DHTXB2 concentrations ($r=-0.39$ and $r=-0.33$, $p < 0.01$). There was no relation of ACA to prothrombin fragments.

CONCLUSION: Increased IgA-ACA levels are associated with low platelet activity and increased ischaemic burden in patients with stable angina. IgA-ACA are related with the extent of daily life ischaemia likely, because they cause endothelial dysfunction after binding on the cell surface and thus, lead to reduced nitric oxide levels and transient reduction of coronary blood flow.

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Clinical Impact of Selective Spasm Provocation Tests: Comparisons Between Acetylcholine and Ergonovine in 1,508 Consecutive Examinations

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Backgrounds: There are few reports regarding the concordance of coronary arterial response between acetylcholine (ACh) and ergonovine (ER) as a spasm provocation test.

Objectives: We compared the coronary arterial response and clinical usefulness between selective intracoronary injection of ACh and intracoronary administration of ER.

Methods and Results: We performed 1508 consecutive selective spasm provocation tests, consisting of 873 acetylcholine (ACh) tests and 635 ergonovine (ER) tests from 1991 to 2002. We examined the frequency of provoked spasms of each agents retrospectively. ACh was injected in incremental doses of 20, 50, and 80 μ g into the right coronary artery and 20, 50, and 100 μ g into the left coronary artery. ER was administered in 10 μ g/min for 4 minutes for a maximal dose of 40 μ g on the right coronary artery and 16 μ g/min over 4 minutes for a total dose of 64 μ g on the left coronary artery. Coronary spasm was defined as transient $> 99\%$ luminal narrowing. Intracoronary ACh provoked spasm in 36.0% of patients and intracoronary ER induced spasms in 29.8% of patients. In patients with ischemic heart disease, the incidence of provoked spasm was not different between ACh tests (50.9%) and ER tests (43.8%). In contrast, the frequency of provoked spasm with ACh tests (11.0%) was significantly higher ($p < 0.05$) than that with ER testings (6.4%) in patients without ischemic heart disease. Moreover, ACh provoked more spasms in patients without fixed stenosis than ER (36.2% vs. 25.5%, $p < 0.01$), and multiple spasms were frequently observed by performing ACh tests (40.0% vs. 27.0%, $p < 0.01$). Major complications, such as ventricular tachycardia, shock or cardiac tamponade, were observed in 1.4% of patients with ACh tests and prolonged spasm was observed in 0.2% of patients with ER tests. The necessity of intracoronary administration of nitroglycerine to relieve coronary spasms during ER testings (5.04%) was frequently observed than that in ACh tests (1.49%). However, no serious irreversible complications, such as death or acute myocardial infarction were observed in this study. **Conclusion:** We concluded that both ACh and ER tests were useful as a spasm provocation test.